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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/190,246	11/13/98	PARRINGTON M	1038-865MIS

HM22/0706

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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1633	13

DATE MAILED: 07/06/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/190,246	Applicant(s) Parrington et al.
	Examiner Wilson, Michael C.	Group Art Unit 1633

☒ Responsive to communication(s) filed on *Apr 13, 2000* .

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-38* is/are pending in the application.

Of the above, claim(s) *3 and 4* is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1, 2, and 5-38* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____ .

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *7*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

The Information Disclosure Statement filed 11-10-99, paper number 7, has been considered and made of record. The additional references filed 2-29-00, paper number 9, which were listed on the IDS filed 11-10-99 have been entered. The references filed 2-29-00 did not come with an additional IDS and is not required.

Response to Amendment

1. The amendments to pages 9, 10, 11 and 20-22 of the instant specification have not been entered because the text described does not appear on the pages listed.

Specification

2. The attempt to incorporate subject matter into this application by reference to US application 08/923558 is improper because the method of immunizing the mice is considered essential to practice the invention. The relevant information regarding the method of immunizing the control group should be included in the instant specification. The results obtained in applications 08/923,558, 08/476,397 and 08/896,500 are not included in the instant specification (page 26, line 22). The comparison of the results obtained in example 3 of the instant invention to the results obtained in another application is essential subject matter; therefore, such results should be included in the specification.

The blanks for US Patent applications (page 23, line 25; page 24, line 23) should be filled in with the appropriate US Patent application number.

The blanks for the ATCC designation and date deposited for pMP42 on page 22, line 12 should be filled in with the appropriate information.

Drawings

3. The corrections to the drawings have been entered.

Claim Objections

4. Claim 16 is objected to because of the following informalities: the word "to" appears twice on line 3.

Claim 11 is objected to because of the following informalities: the word "to" should be inserted after the word adjacent on line 2. Appropriate correction is required.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 2 and 5-38 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for immunogenic compositions and a method of provoking an immune response, does not reasonably provide enablement for vaccine compositions and methods of preventing disease. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The specification details the production of antibodies specific for RSV proteins after immunization of mice with the claimed construct. At no point is the specific antibody response of the mice shown to be protective. The specification states 1 out of 6 mice receiving pMP44 were infected with RSV upon challenge (page 26, line 18) and that only 83% protection was obtained indicating that some infection of the lungs occurred. The protective immune response is the hallmark of a vaccine. The specification does not provide adequate guidance for one of skill to obtain protection against RSV challenge such that vaccine or protective embodiments are enabled. As such, claims drawn to vaccine compositions or methods of preventing diseases caused by paramyoxviruses are not enabled. The composition claims are included in this rejection as they relate to how to use such compositions and not how to make such compositions.

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 2 and 5-38 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 1, the phrase " a protein or protein fragment that generates antibodies that specifically react with the paramyoxovirus protein" is unclear because a protein or protein fragment does not generate anything. An immunogenic protein or peptide can induce antibody production by the immune system but does not generate the antibodies by itself.

Claim 5 is dependent on claim 4 which is not under consideration in the instant invention. Dependency to an elected claim or cancellation of claim 5 is required.

The phrase "identifying characteristics of plasmid pMP44" in claims 18, 21, 33 and 37 is indefinite because the specification does not teach the characteristics that identify pMP44 and such characteristics cannot be determined. Therefore, the metes and bounds of the characteristics included in such a limitation cannot be determined.

The term "adjacent" in claim 11 is indefinite. It is unclear whether the term is intended to mean the 3rd sequence is directly adjacent to the 2nd sequence or is operatively linked in a nearby location in relation to the 2nd sequence.

The phrase "to enhance the immunoprotective ability of a paramyxovirus protein" (claim 11) is indefinite because the it is unclear which proteins have immunoprotective ability and which sequence enhance such ability. While some paramyxovirus proteins may induce an immune response that provides protection against viral challenge, it is not clear how such an effect

correlates to immunoprotective ability of a paramyxovirus protein. Since it is unclear what applicants consider the immunoprotective ability of a protein, it cannot be determined when such an ability has been enhanced.

The phrase "when expressed *in vivo* from the vector in a host" (claim 11) is unclear. It is unclear whether "from the vector" refers to the protein or the expression. It is unclear whether "in a host" refers to the presence of a vector in a host, a protein in a host or expression that occurs in a host.

The term "substantially" in claim 12 is indefinite because the metes and bounds of what applicants consider "substantial" amounts of transcribed mRNA cannot be determined.

The phrase "all transcribed mRNA from the vector region administration encodes the RSV protein" (claim 12) is unclear. The term administration appears to be out of place and the meaning of the phrase cannot be determined.

The phrase "aberrant mRNA splicing, *in vivo*" is indefinite because it is unclear whether applicants intend to distinguish aberrant mRNA splicing *in vivo* from mRNA splicing *in vitro* or whether applicants are merely indicating that aberrant mRNA splicing does not occur when the vector is used *in vivo*.

The use of the term "has" in claims 19, 22, 31, 34 and 38 is indefinite because a vector does not have possession of SEQ ID NO:X. A vector comprises/consists of/has a nucleic acid sequence of SEQ ID NO:X.

Claims 20-22 are indefinite because the claim is directed toward immunizing a host against disease but does not result in immunization. The step of administration does not necessarily result in obtaining immunization. The body of the claim should reflect the preamble of the claim.

Claims 23-31 are indefinite because the claim is directed toward using a gene to protect against disease but does not result in protection. The step of introducing the vector does not necessarily result in protecting against disease. The body of the claim should reflect the preamble of the claim.

Claims 32 is indefinite because the claim is directed toward producing a vaccine for protection of a host against disease but the claim does not result in obtaining a vaccine with such a use. The body of the claim should reflect the preamble of the claim.

Claim 33 is drawn to a composition of claim 32; however, claim 32 is drawn to a method. It is unclear what applicants intend to claim.

The phrase "immunoeffective amount" in claim 36 is indefinite because the specification does not define what applicants consider such an amount and such an amount cannot be determined in the art. Therefore, the metes and bounds of what applicants consider "immunoeffective amount" cannot be determined.

The phrase "capable of" in claim 23 is indefinite because it is unclear whether the protein or fragment does generate antibodies. "Capable of" implies a latent property and the conditions for obtaining the latent property must be clearly defined. The claims do not clearly recite the

conditions for obtaining such a property. Therefore, it is unclear if the latent property is ever obtained.

Claim 21 is indefinite because it is dependent upon itself.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 1, 2, 8, 9, 11-13, 18, 20, 21, 32, 33, 35, 36 and 37 are rejected under 35 U.S.C. 102(e) as being anticipated by Dubensky et al. (US Patent 5,814,482, Sept. 29, 1998).

Dubensky et al. teach an alphavirus expression vector for the expression of heterologous sequences. The vectors can encode RSV proteins as in claims 10 and 22. Semliki forest virus is a contemplated alphavirus (column 11, line 67). Dubensky et al. discloses using the above vectors to induce an immune response in a mammal. The Semliki forest virus taught by Dubensky et al. is equivalent to the sequence contained in plasmid pSFVI (claim 9). The limitation of a third sequence located adjacent to the first sequence and between the first sequence and the promoter (claims 11-13) is equivalent to the DNA sequence adjacent to the alphavirus sequence and the DNA sequence between the alphavirus sequence and the promoter taught by t Dubensky et al.

Such a sequence comprises a "pair of splice sites" because the sequence can be spliced at any two sites. The phrases "to enhance the immunoprotective ability" and "to prevent aberrant mRNA splicing" are intended uses and do not bear patentable weight when considering art rejections. The vector taught by Dubensky et al. has the identifying characteristics of pMP44 in that they both are alphaviruses encoding RSV proteins (claim 18, 21, 33 and 37). The limitation of "from which the transmembrane anchor and cytoplasmic tail may be absent" (claim 32) does not bear patentable weight because the anchor and tail may be present or absent. Therefore, Dubensky et al. anticipate the claimed invention.

8. Claims 1, 2, 5-16, 18, 20, 21, 23-30, 32, 33, 35, 36 and 37 are rejected under 35 U.S.C. 102(e) as being anticipated by Parrington (US Patent 6,060,308, May 9, 2000).

Parrington et al. teach a Semliki forest viral vector for the expression of the F or G proteins of RSV. The sequence may contain the CMV immediate early promoter and rabbit β-globin intron II (column 4, line 11). The vector can be administered *in vivo* to induce an immune response. Thus, Parrington et al. anticipate the claims.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 2, 5-16, 18, 20, 21, 23-30, 32, 33, 35, 36 and 37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dubensky et al. (US Patent 5,814,482, Sept. 29, 1998) in view of Li et al. (WO 96/40945, Dec. 19, 1996).

Dubensky et al. teach an alphavirus expression vector for the expression of heterologous sequences. The vectors can encode RSV proteins as in claims 10 and 22. Semliki forest virus is a contemplated alphavirus (column 11, line 67). The Semliki forest virus taught by Dubensky et al. is equivalent to the sequence contained in plasmid pSFVI (claim 9). Dubensky et al. discloses using the above vectors to induce an immune response in a mammal. Dubensky et al. teach the vector can include a hepatitis delta virus ribozyme (HDV) (column 71, line 15). The limitation of a third sequence located adjacent to the first sequence and between the first sequence and the promoter (claims 11-13, 27 and 28) is equivalent to the DNA sequence adjacent to the alphavirus sequence and the DNA sequence between the alphavirus sequence and the promoter taught by t Dubensky et al. Any DNA sequence comprises a "pair of splice sites" because the sequence can be spliced at any two sites. The phrases "to enhance the immunoprotective ability" and "to prevent aberrant mRNA splicing" are intended uses and do not bear patentable weight when considering art rejections. The limitation of "from which the transmembrane anchor and cytoplasmic tail may be absent" (claim 32) does not bear patentable weight because the anchor and tail may be present or absent. Dubensky et al. does not teach the nucleic acid sequence of the RSV F or G proteins.

However, at the time of filing, Li et al. teach a vector encoding the RSV F and G proteins under the control of the CMV immediate early promoter and comprising the rabbit globin intron II (page 14, lines 5-21).

Thus, it would have been obvious to one of ordinary skill in the art at the time the invention was made to use the expression vector encoding RSV proteins taught by Dubensky et al. to deliver the F or G protein taught by Li et al. Motivation is provided by Li et al. by stating that the F or G proteins may be used to induce an immune response (page 15, line 17). It would have been obvious to one of skill in the art at the time of filing to put the rabbit β-globin intron II sequence between the alphavirus sequence and the CMVIE promoter to enhance transcription/translation and increase *in vivo* expression as suggested by Li et al. (page 14, line 10). The vector taught by Dubensky et al. has the identifying characteristics of pMP44 in that they both are alphaviruses encoding RSV F under the control of the CMVIE promoter operatively linked to the rabbit β-globin intron between the alphavirus sequence and the CMVIE promoter (claim 18, 21, 30, 33 and 37). It would have been obvious to one of ordinary skill in the art at the time the invention was made to place the HDV ribozyme on the 3' end of the alphavirus sequence to insure deletion of the polyA termination sequence as suggested by Dubensky et al. (column 71, line 17) who also place the HDV ribozyme on the 3' end of the alphavirus sequence.

Therefore, Applicants' claimed invention as a whole is *prima facie* obvious in the absence of evidence to the contrary.

Double Patenting

10. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 2, 5-16, 18, 20, 21, 23-30, 32, 33 and 35-37 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1- of U.S. Patent No. 6,060,308. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims encompass vectors lacking a Sei restriction site and the pMP37 vector claimed in 6,060,308. The pMP37 vector is disclosed in the instant application on page 22, line 10 and in Fig. 1B, top left which according to U.S. Patent 6,060,308 lacks a SpeI restriction site (claims 1 and 8). Any of the vectors disclosed in the instant invention could be linearized by SpeI restriction and lack a Spe I restriction site which is taught on page 24, line 24 and would be obvious to one of ordinary skill in the art at the time of the invention. Therefore, claims 1, 2, 5-16, 18, 20, 21, 23-30, 32, 33 and 35-37 of the instant invention are obvious in view of claims 1-3, 5, 6, 8, 18-23 and 26 of US Patent 6,060,308.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael C. Wilson whose telephone number is (703) 305-0120. The examiner can normally be reached on Monday through Friday from 8:30 am to 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader, can be reached on (703) 308-0447. The fax phone number for this Group is (703) 308-8724.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 305-0196.

Michael C. Wilson

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